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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,766	02/04/2004	Vivekananda M. Vrudhula	CT 2662 DIV2	3679

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 12/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,766	VRUDHULA ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19* is/are allowed.

6)☒ Claim(s) *1-5,8-18 and 20* is/are rejected.

7)☒ Claim(s) *6 and 7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-29-04*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *attached* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is a divisional of 10/044,183 (now U.S. 6,888,004). A restriction requirement was issued in parent application of 10/044,183. The current claims are drawn to the subject matter of Groups I and III of the restriction in application 10/ 044,183.

A telephone call was made to Mr. Shah Makujina on 12-02-05 to request an election. Mr. Makujina elected Group I (wherein R^1, R^2, X=Y, and A together form a **tetrahydro-imidazo[1,2-a]-pyrimidinyl**).

Claims 1-20 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-5, 8-18 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 recites R^2 as D'-D"(R^3)(R^4) with indefinite metes and bounds because when D' is a bond, it is not clear if there is a double bond between Y and D". The chemical structure; however, only allows a single bond between R^2 and Y. Furthermore, when D" is C-OH or CH, and said C is bonded to D' while double bonded to R^3 or R^4, then said C appears to have five bonds.

b. Claims 2-5, 8-18 and 20 are rejected as being dependent on claim 1, and carrying over the indefinite limitation of R^2.

c. Claim 20 is also rejected for reciting limitations of "*yet other disorders requiring neuroprotection*", which has indefinite metes and bounds as to what disorders are intended. It also recites disorders with conflicting symptoms such as: eating disorders (e.g., anorexia and bulimia) vs. obesity; depression vs. anxiety; insomnia vs. other sleep disorders, etc.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claim 20 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating *anxiety*, does not reasonably provide enablement for a method of treating other diseases allegedly related to CRF-1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 20 recites:

> **20**. A method of treating depression, anxiety, affective disorders, post-traumatic stress disorder, post-operative stress, headache, drug addiction, eating disorders and obesity, sudden death due to cardiac disorders, iritable bowel syndrome, hypertension, syndrome X, inflammatory disorders, stress-induced immune suppression, infertility, stress-induced insomnia and other sleep disorders, seizures, epilepsy, stroke and cerebral ischemia, traumatic brain injury, yet other disorders requiring neuroprotection, drug or alcohol withdrawal symptoms, other disorders including tachycardia, congestive heart failure, osteoporosis, premature birth, psychosocial dwarfism, ulcers, diarrhea and post-operative ileus comprising the administration of a pharmaceutical composition comprising a compound according to claim 1.

The scope of claim 20 covers the treatment of diseases that affecting various organs or systems such as: CNS, cardiovasculart, reproductive system, GI, bones, joints, etc. Furthermore, some of said diseases have conflicting symptoms (e.g., depression vs. anxiety, or

obesity vs. anorexia). Said claim also covers unknown diseases as suggested by the limitation "yet other disorders requiring neuroprotection". Clearly, the scope of claim 20 is unduly broad.

The amount of direction or guidance presented:

The specification only provides *in-vitro* data for numerous compounds and their K_i value to show the antagonistic activity said compounds have on CRF-1 receptor . However, there is no evidence if the tested compounds are effective in treating depression, obesity, sudden death due to cardiac disorders, hypertension, epilepsy, stroke, etc. All of the diseases recited in claim 16 have different underlying factors, and manifestation. Some even have conflicting symptoms. Thus, with mere *in-vitro* data provided, the specification fails to provide sufficient guidance for a skilled clinician to treat any listed diseases other than anxiety based on the known activity of CRF on the basal and stress-release of adrenocorticotropic hormone.

The state of the prior art:

As acknowledged in the specification, CRF-1 is "a primary mediators of stress- and anxiety-related physiological responses in humans and other mammals by stimulating ACTH secretion from the anterior pituitary gland" Therefore, it would be reasonable to expect CRF-1 antagonists like the claimed compounds to treat anxiety. However, regarding other diseases, there is no crucial evidence that CRF could affect cardiovascular diseases, eating disorders, obesity, depression, affective disorders, inflammatory diseases, premature birth, sudden death, etc. Furthermore, there is no one agent that can treat obesity and eating disorders which includes anorexia and bulimia. Likewise, a CRF-1 antagonist cannot simultaneously treat both depression

and anxiety depression since they have opposite symptoms. Thus, the state of the art does not support the scope of claim 20.

The relative skill of those in the art:

Even with the advanced training, the skilled clinician would have to engage in undue experimentation to establish data that would adequately support the use of the claimed compounds in the treatment of many diseases that are allegedly related to CRF including those recited in claim 20. Such a task would require a tremendous amount of effort, time and resources.

The predictability or unpredictability of the art & The quantity of experimentation necessary:

The pharmaceutical art has been known for its unpredictability due to various conflicting path ways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only provides *in-vitro* data for CRF-1 antagonistic activity without showing any *in-vivo* data that could substantiate the treatment of many diseases associated with CRF-1. Such a description alone does not adequately guide the skilled clinician to treat diseases other than *anixiety*. Thus, with such a limited teaching, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the methods recited in claim 20.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 9, 10 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by **Satow et. al.** (EP 970,958 A1- cited on IDS). Page 48 of EP'958 lists two compounds on line 35 that read on compounds of the above claims. Page 51 also list a compound (the left compound) that reads on a compound of the above claims. The disclosed compounds read on the instantly claimed formula I with the following substituents:

i. X is C; Y is C;

ii. X^1 is N; Y^1 is N;

iii. Y^2 is CR^5 and is double bonded to J;

iv. J is CH; Z^1 is C(O);

v. R^5 is haloalkyl;

vi. R^1 is hydrogen;

vii. R^2 is D'-D"(R^3)(R^4);

viii. D' is CH_2 or a bond;

ix. D" is CH;

x. Both R^3 and R^4 are hydrogen.

Claim Objections

4. Claims 6 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claims depend on claim 1, but recite R^2 as being $C(D)NR^3R^4$, or $CH_2NR^3R^4$ which is not indefinite, and not taught by the prior arts of record.

Allowable Subject Matter

4. Claim 19 is allowable.

The following is a statement of reasons for the indication of allowable subject matter:

Claim 19 is independent, and recites species of 8H-1,3a,8-triaza-cyclopenta[a]indene, which are not taught or fairly suggested by the prior arts of record.

References cited on PTO-892

5. The cited references show state of the art only as they fail to teach or fully suggest a tricyclic compound substituted with a substituent corresponding to the instant R^2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tamthom N. Truong
Examiner
Art Unit 1624

12-02-05

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